Clinical trial results:
A Phase 2, Open-label Extension Study to Evaluate Long-term Safety of MEDI-546 in Adults with Systemic Lupus Erythematosus

Summary

EudraCT number	2012-004619-30
Trial protocol	CZ HU BG
Global end of trial date	18 July 2018

Results information

Result version number	v1 (current)
This version publication date	17 July 2019
First version publication date	17 July 2019

Trial information

Trial identification

Sponsor protocol code	CD-IA-MEDI-546-1145

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01753193
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	MedImmune Way, Gaithersburg, Maryland, United States, 20878
Public contact	Raj Tummala, MedImmune, LLC, +1 301-398-0548, information.center@astrazeneca.com
Scientific contact	Raj Tummala, MedImmune, LLC, +1 301-398-0548, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the long-term safety and tolerability of intravenous (IV) MEDI-546 in adult participants with moderately-to-severely active systemic lupus erythematosus (SLE).

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 March 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	United States: 67
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Peru: 40
Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Colombia: 34
Country: Number of subjects enrolled	Mexico: 13
Worldwide total number of subjects	218
EEA total number of subjects	42

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	210
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 28 Mar 2013 to 18 Jul 2018.

Pre-assignment

Screening details:

A total of 218 participants were enrolled in this open-label extension (OLE) study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Anifrolumab

Arm description:

Participants received intravenous (IV) infusion of anifrolumab (MEDI-546) 1000 milligrams (mg) every 4 weeks (Q4W) from Day 1 (Week 0) until 12-Feb-2015 (approval of protocol amendment 4); and thereafter received 300 mg Q4W for up to 3 years or until the sponsor discontinued development of anifrolumab, whichever came first.

Arm type	Experimental
Investigational medicinal product name	Anifrolumab
Investigational medicinal product code	MEDI-546
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of anifrolumab (MEDI-546) 1000 milligrams (mg) every 4 weeks (Q4W) from Day 1 (Week 0) until 12- Feb-2015 (approval of protocol amendment 4); and thereafter 300 mg Q4W for up to 3 years or until the sponsor discontinued development of anifrolumab, whichever came first.

Number of subjects in period 1	Anifrolumab
Started	218
Completed	172
Not completed	46
Adverse event, serious fatal	1
Consent withdrawn by subject	23
Unspecified	16
Lost to follow-up	6

Baseline characteristics

Reporting groups	
Reporting group title	Anifrolumab
Reporting group description:	
Participants received intravenous (IV) infusion of anifrolumab (MEDI-546) 1000 milligrams (mg) every 4 weeks (Q4W) from Day 1 (Week 0) until 12-Feb-2015 (approval of protocol amendment 4); and thereafter received 300 mg Q4W for up to 3 years or until the sponsor discontinued development of anifrolumab, whichever came first.	

Reporting group values	Anifrolumab	Total	
Number of subjects	218	218	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	210	210	
From 65-84 years	8	8	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	40.8		
standard deviation	± 12.2	-	
Sex: Female, Male Units: Subjects			
Male	15	15	
Female	203	203	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	104	104	
Not Hispanic or Latino	114	114	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	4	
Asian	11	11	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	29	29	
White	87	87	
More than one race	2	2	
Unknown or Not Reported	85	85	

End points

End points reporting groups

Reporting group title	Anifrolumab

Reporting group description:

Participants received intravenous (IV) infusion of anifrolumab (MEDI-546) 1000 milligrams (mg) every 4 weeks (Q4W) from Day 1 (Week 0) until 12-Feb-2015 (approval of protocol amendment 4); and thereafter received 300 mg Q4W for up to 3 years or until the sponsor discontinued development of anifrolumab, whichever came first.

Primary: Number of Particpants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Particpants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event is any AE that resulted in death, life threatening, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, is a congenital anomaly/birth defect in offspring of a study participant, is an important medical event that may jeopardize the participant or may require medical intervention. TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study.

End point type	Primary

End point timeframe:

From first dose of study drug (Day 1) through 168 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	218			
Units: Participants				
TEAEs	170			
TESAEs	50			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events Resulting in Discontinuation (DAEs) of Anifrolumab

End point title	Number of Participants With Adverse Events Resulting in Discontinuation (DAEs) of Anifrolumab[2]

End point description:

Number of participants with DAEs are reported. As-treated population was analysed for this endpoint,

which included all participants who received any dose of study drug in the OLE study.

End point type	Primary

End point timeframe:

From first dose of study drug (Day 1) through 168 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	218			
Units: Participants	17			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Adverse Events of Special Interest (AESIs)[3]

End point description:

An AESI is scientific and medical concern specific to understanding of the study drug. An AESI may be serious or non-serious. Number of participants with AESIs are reported. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study.

End point type	Primary

End point timeframe:

From first dose of study drug (Day 1) through 168 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	218			
Units: Participants				
Herpes zoster	11			
Drug hypersensitivity	1			
Hypersensitivity	2			
Infusion related reaction	4			
Nausea	1			
Hodgkin's disease	1			
Latent tuberculosis	5			
Hypersensitivity vasculitis	1			
Vasculitis	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Drug Antibodies (ADA) Titer to Anifrolumab

End point title	Number of Participants With Positive Anti-Drug Antibodies (ADA) Titer to Anifrolumab

End point description:

The number of participants with positive serum antibodies to anifrolumab at anytime (including baseline) are reported. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study. Participants with reportable ADA titer results were analysed for this end point.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose on Day 1) up to Week 168

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	216			
Units: Participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibodies (ADA) Titer to Anifrolumab

End point title	Anti-Drug Antibodies (ADA) Titer to Anifrolumab

End point description:

Median ADA titer in participants with ADA-positive assessments and reportable ADA titer results are reported. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study. Only participants who had ADA-positive assessments with reportable ADA titer results were analysed for this end point.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose on Day 1) up to Week 168

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Antibody titers				
median (full range (min-max))	120 (30 to 120)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of ADA-positive Participants With Decreased Serum Concentration of Anifrolumab

End point title	Number of ADA-positive Participants With Decreased Serum Concentration of Anifrolumab

End point description:

Number of participants with decreased serum concentration of anifrolumab due to the ADA-positive results are reported. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study. Only participants who had ADA-positive assessments with reportable ADA titer results were analysed for this end point.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose on Day 1) up to Week 168

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of ADA-positive Participants With Decreased Pharmacodynamics Response of Anifrolumab

End point title	Number of ADA-positive Participants With Decreased Pharmacodynamics Response of Anifrolumab

End point description:

Number of participants with decreased pharmacodynamic response of anifrolumab due to ADA-positive results are reported. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study. Only participants who had ADA-positive assessments with reportable ADA titer results were analysed for this end point.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose on Day 1) up to Week 168

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) Global Score for ADA Positive Participants

End point title	Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) Global Score for ADA Positive Participants

End point description:

The SLEDAI-2K is an activity index that measures disease activity and records feature of active lupus as present or not present. SLEDAI-2K uses a weighted checklist to assign a numerical score based on the presence or absence of 24 symptoms. Each symptom present is assigned between 1 and 8 points based on its usual clinical importance, yielding a total score that ranges from 0 points (no symptoms) to 105 points (presence of all defined symptoms). As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study. Only participants who had ADA-positive assessments with reportable ADA titer results were analysed for this end point. Here 'n' denotes number of participants analysed for specified time point.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose on Day 1); and Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 160, and 168

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Units on Score				
arithmetic mean (standard deviation)				
Baseline (n= 5)	7.8 (± 7.6)			
Week 12 (n= 4)	5 (± 2.0)			
Week 24 (n= 4)	1.5 (± 1.9)			
Week 36 (n= 4)	2.0 (± 2.3)			
Week 48 (n= 5)	1.8 (± 2.0)			
Week 60 (n= 4)	2.0 (± 1.6)			
Week 72 (n= 2)	4.0 (± 5.7)			
Week 84 (n= 2)	3.0 (± 1.4)			
Week 96 (n= 2)	3.0 (± 1.4)			
Week 108 (n= 2)	4.0 (± 0.0)			
Week 120 (n= 2)	5.0 (± 1.4)			
Week 132 (n= 2)	4.0 (± 0.0)			
Week 144 (n= 2)	7.0 (± 7.1)			

Week 156 (n= 2)	6.0 (± 2.8)			
Week 160 (n= 2)	2.0 (± 2.8)			
Week 168 (n= 2)	2.0 (± 2.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of ADA-positive Participants With TEAEs and TESAEs

End point title	Number of ADA-positive Participants With TEAEs and TESAEs

End point description:

The number of ADA-positive participants with TEAEs and TESAEs are reported. As-treated population was analysed for this endpoint, which included all participants who received any dose of study drug in the OLE study. Only participants who had ADA-positive assessments with reportable ADA titer results were analysed for this end point.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose on Day 1) up to Week 168

End point values	Anifrolumab			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
TEAEs	5			
TESAEs	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug (Day 1) through 168 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Anifrolumab Total

Reporting group description:

Participants received intravenous (IV) infusion of anifrolumab (MEDI-546) 1000 milligrams (mg) every 4 weeks (Q4W) from Day 1 (Week 0) until 12-Feb-2015 (approval of protocol amendment 4); and thereafter received 300 mg Q4W for up to 3 years or until the sponsor discontinued development of anifrolumab, whichever came first.

Serious adverse events	Anifrolumab Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	50 / 218 (22.94%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis superficial			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
High risk pregnancy			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cyst			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Cervical polyp			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysfunctional uterine bleeding			

subjects affected / exposed	2 / 218 (0.92%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metrorrhagia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pleural effusion				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary infarction				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericarditis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Idiopathic intracranial hypertension			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Syncope			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Oesophageal ulcer			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrotic syndrome			

subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothalamic pituitary adrenal axis suppression			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Spinal column stenosis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Systemic lupus erythematosus			
subjects affected / exposed	5 / 218 (2.29%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chikungunya virus infection			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Latent tuberculosis			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mastoiditis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	1 / 1		
Pneumonia bacterial			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural infection			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Anifrolumab Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	164 / 218 (75.23%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of bone			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Melanocytic naevus			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Seborrhoeic keratosis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Skin papilloma			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Squamous cell carcinoma of the cervix			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Uterine leiomyoma			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Vulvovaginal warts			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	2		
Peripheral coldness			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	2		
Peripheral venous disease			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Raynaud's phenomenon			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Vasculitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	4 / 218 (1.83%) 4		
Acquired gene mutation subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Cyst subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Influenza like illness subjects affected / exposed occurrences (all)	6 / 218 (2.75%) 10		
Oedema peripheral subjects affected / exposed occurrences (all)	4 / 218 (1.83%) 4		
Pyrexia subjects affected / exposed occurrences (all)	5 / 218 (2.29%) 5		
Tenderness subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 3		
Hypersensitivity subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2		
Seasonal allergy subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2		
Reproductive system and breast disorders Breast discharge subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 2		
Breast tenderness			

subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Cervical dysplasia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Cervical polyp				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Dysmenorrhoea				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Dyspareunia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Endometrial hyperplasia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Endometrial thickening				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Endometriosis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Erectile dysfunction				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Menometrorrhagia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Menorrhagia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Menstruation delayed				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Menstruation irregular				

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Ovarian cyst			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Pelvic pain			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Polymenorrhoea			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Uterine cervical erosion			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Uterine haemorrhage			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Uterine polyp			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Vaginal discharge			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Vulvovaginal dryness			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Bronchial hyperreactivity			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Catarrh			

subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Cough				
subjects affected / exposed	5 / 218 (2.29%)			
occurrences (all)	5			
Dysphonia				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Emphysema				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Nasal congestion				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Oropharyngeal pain				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pleurisy				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Productive cough				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pulmonary fibrosis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Reflux laryngitis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Rhinitis allergic				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Rhinorrhoea				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Sinus congestion				

subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Snoring			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	2		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Bipolar disorder			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	4		
Libido decreased			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Blood immunoglobulin a decreased				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Blood potassium decreased				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Electrocardiogram qt shortened				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Hepatic enzyme increased				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Lipids abnormal				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Liver function test increased				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Mycobacterium tuberculosis complex test positive				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Neutrophil count increased				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	4			
Nuclear magnetic resonance imaging brain abnormal				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Transaminases increased				

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Burns second degree			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Compression fracture			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	5 / 218 (2.29%)		
occurrences (all)	5		
Epicondylitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Head injury			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	9		
Injection related reaction			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Joint dislocation			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Limb injury			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	5		
Rib fracture			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Scar			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Bifascicular block			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Bundle branch block right			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Coronary artery disease			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Left atrial dilatation			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		

Myocardial fibrosis subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Palpitations subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2			
Supraventricular tachycardia subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2			
Tachycardia subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2			
Ventricular extrasystoles subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Nervous system disorders				
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Cerebrovascular disorder subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Dizziness subjects affected / exposed occurrences (all)	5 / 218 (2.29%) 6			
Encephalopathy subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Headache subjects affected / exposed occurrences (all)	14 / 218 (6.42%) 21			
Hypersomnia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Intercostal neuralgia				

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Ischaemic stroke			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Lumbosacral radiculopathy			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	6		
Paraesthesia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Pineal gland cyst			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Seizure			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	4		
Visual field defect			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 218 (2.75%)		
occurrences (all)	6		
Hyperleukocytosis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Hypercoagulation			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		

Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Leukaemoid reaction subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Leukocytosis subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 6		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Neutropenia subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2		
Neutrophilia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Thrombocytosis subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 2		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2		
Eustachian tube dysfunction subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Tympanic membrane perforation subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Eye disorders Blepharitis subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Blepharochalasis			

subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Cataract			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	4		
Chalazion			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Eyelid oedema			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Macular degeneration			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Myopia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Scleritis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Visual acuity reduced			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	5 / 218 (2.29%)		
occurrences (all)	6		
Aphthous ulcer			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		

Chronic gastritis subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2			
Constipation subjects affected / exposed occurrences (all)	5 / 218 (2.29%) 5			
Dental caries subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Diarrhoea subjects affected / exposed occurrences (all)	11 / 218 (5.05%) 12			
Dyspepsia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Enteritis subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Gastric mucosa erythema subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Gastric ulcer subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2			
Gastritis subjects affected / exposed occurrences (all)	7 / 218 (3.21%) 7			
Gastrointestinal angiodysplasia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Gingival bleeding subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1			

Hiatus hernia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Internal hernia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Irritable bowel syndrome			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	7 / 218 (3.21%)		
occurrences (all)	8		
Noninfective gingivitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Pancreatitis chronic			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Hepatic steatosis			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
Hypertransaminasaemia			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Actinic keratosis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Dermatitis contact			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Drug eruption			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Hair growth abnormal			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Hypersensitivity vasculitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Idiopathic urticaria			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Keratosis pilaris			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Mechanical urticaria			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Panniculitis			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		

Rash			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	3		
Skin discolouration			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	4		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Hypertonic bladder			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Nephritis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Nephrolithiasis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Ureterolithiasis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Hyperparathyroidism primary			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Thyroid mass			

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	7 / 218 (3.21%)		
occurrences (all)	8		
Bursitis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Fibromyalgia			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Foot deformity			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Joint swelling			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	7 / 218 (3.21%)		
occurrences (all)	7		
Musculoskeletal stiffness			

subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Myalgia				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
Myofascial pain syndrome				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Myositis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Neck pain				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
Osteoarthritis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Osteochondritis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Osteonecrosis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	4			
Osteopenia				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Osteoporosis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Pain in extremity				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Rotator cuff syndrome				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	4			
Scoliosis				

subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Spondylolisthesis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Tendonitis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	3		
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Acarodermatitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Appendicitis			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Bacterial vaginosis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Body tinea			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Bone abscess			
subjects affected / exposed	1 / 218 (0.46%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	28 / 218 (12.84%)		
occurrences (all)	33		

Bronchitis bacterial				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Bronchitis viral				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Candida infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Cellulitis				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	8			
Cervicitis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Conjunctivitis				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
Cystitis				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
Dermatophytosis of nail				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Ear infection				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Furuncle				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	4			
Gastroenteritis				
subjects affected / exposed	5 / 218 (2.29%)			
occurrences (all)	6			
Gastroenteritis viral				
subjects affected / exposed	4 / 218 (1.83%)			
occurrences (all)	4			

Gastrointestinal viral infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Genital candidiasis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Genital herpes simplex				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Herpes simplex				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Herpes zoster				
subjects affected / exposed	10 / 218 (4.59%)			
occurrences (all)	10			
Infected bite				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	9 / 218 (4.13%)			
occurrences (all)	10			
Latent tuberculosis				
subjects affected / exposed	5 / 218 (2.29%)			
occurrences (all)	5			
Lymphangitis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Nail infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	32 / 218 (14.68%)			
occurrences (all)	40			
Onychomycosis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			

Oral candidiasis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	3			
Oral herpes				
subjects affected / exposed	6 / 218 (2.75%)			
occurrences (all)	7			
Oropharyngeal candidiasis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Otitis media				
subjects affected / exposed	4 / 218 (1.83%)			
occurrences (all)	4			
Papilloma viral infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Paronychia				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Parotitis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pelvic inflammatory disease				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Peritonsillar abscess				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	10 / 218 (4.59%)			
occurrences (all)	11			
Pharyngitis streptococcal				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
Pharyngotonsillitis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			

Pleurisy viral				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	4 / 218 (1.83%)			
occurrences (all)	6			
Pneumonia bacterial				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pulpitis dental				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Pyelonephritis acute				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	8 / 218 (3.67%)			
occurrences (all)	12			
Skin candida				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Skin infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Streptococcal infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Subcutaneous abscess				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	3			

Tinea manuum				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Tonsillitis				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			
Tracheobronchitis				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	20 / 218 (9.17%)			
occurrences (all)	29			
Urinary tract infection				
subjects affected / exposed	13 / 218 (5.96%)			
occurrences (all)	17			
Urinary tract infection fungal				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Vaginal infection				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Viral infection				
subjects affected / exposed	5 / 218 (2.29%)			
occurrences (all)	5			
Viral upper respiratory tract infection				
subjects affected / exposed	5 / 218 (2.29%)			
occurrences (all)	6			
Vulval abscess				
subjects affected / exposed	1 / 218 (0.46%)			
occurrences (all)	1			
Vulvovaginal candidiasis				
subjects affected / exposed	2 / 218 (0.92%)			
occurrences (all)	2			
Vulvovaginal mycotic infection				
subjects affected / exposed	3 / 218 (1.38%)			
occurrences (all)	3			

Vulvovaginitis subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Zika virus infection subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Metabolism and nutrition disorders Acquired mixed hyperlipidaemia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Hyperlipidaemia subjects affected / exposed occurrences (all)	2 / 218 (0.92%) 2		
Hypokalaemia subjects affected / exposed occurrences (all)	5 / 218 (2.29%) 6		
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Malnutrition subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		
Vitamin d deficiency subjects affected / exposed occurrences (all)	1 / 218 (0.46%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2013	Summary of clinical experience was revised to remove the explanation regarding the last day and the first day of the study. Overview of study design was revised to include the explanation that once participants complete treatment and follow-up in the study, signed the informed consent form (ICF), and met all study eligibility criteria, they may be enrolled in this OLE study. Estimated duration of participant's participation and treatment regimen sections in the study were revised to reduce the duration of the study to 2 years. Rationale for study design was updated to remove the reference to participants at least 18 years of age. Inclusion criteria clarified use of adequate contraception for females and males, clarified to state that participants must be willing to forgo other forms of experimental treatment. Withdrawal criteria was clarified for procedures following permanent discontinuation of study drug. Monitoring of dose administration was updated to remove the reference that temperature should be taken orally. Schedule of study procedures for the treatment period and for 85-day follow-up period were revised and updated. Removal of Clinical Evaluation Questionnaire for adverse event of special interest (AESI), addition of procedures for an unscheduled study visit, collection of biomarker samples was made optional, addition of statement that non-serious and serious AESIs should be recorded.
01 April 2013	Addition of Health-related quality of life impact as exploratory objective and addition of SF-36v2 assessments and analyses to relevant sections, clarification of management of oral corticosteroid (OCS) treatment, addition of hepatitis B virus DNA polymerase chain reaction, QuantiFERON-TB Gold In-tube systemic lupus erythematosus test, immunology profile, urinalysis, urine β human chorionic gonadotropin, and investigator flare question(s) to visit 27, clarification regarding recording of serious and non-serious events of hepatic abnormality as well as AESIs (new or reactivated TB infection, herpes zoster infection, malignancy, infusion, hypersensitivity or anaphylactic reactions, and vasculitis).
26 March 2014	Duration of IV infusion updated to approximately 60 minutes, updated that for OCS medication taken >40 mg/day of prednisone (or equivalent) for greater than 14 days, dosing with study medication must be withheld until OCS medication can be tapered to ≤40 mg/day, changes in instructions of dose preparation and monitoring of dose administration, modification in schedule of study procedures to state that if Day 1 of the study occurred on Day 422 of study 1013, many of the procedures/assessments only needed to be collected once. If >28-day window elapsed after Day 422, the Day 1 procedures needed to be conducted, serum sample collection of proteomics/biomarkers made optional, guidance for participant who have had recent contact or show signs and symptoms of active tuberculosis (TB), discontinuation of participants due to active TB or noncompliance with latent TB treatment, guidance for pregnancy testing requirements updated.
12 February 2015	Exemption of participants from requirement of study 1013 completion in regions of Ukraine, interim analysis of study 1013 updated after completion and resulted change in: dose from 1000 mg to 300 mg, infusion time from approximately 60 minutes to at least 30 minutes, and infusion volume based on dose reduction, change in duration of study drug administration from 2 to 3 years, total number of participants randomized in study 1013 (n=307) updated, clarification of permitted study medications and dosing regimens for OCS, clarification that vital signs were to be measured until stable and participant judged by investigator ready for discharge, modification of multiple procedures in the schedule of study assessment, clarification of methodology for multiple study assessments, correction of definition of grade 4 adverse event severity, addition of appendix providing guidance for abnormal liver function test management.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported